

Remarks

Reconsideration of this Application is respectfully requested.

Claims 1, 2, 4, 5, 7-13, 18 and 19 are sought to be amended, and claim 6 is sought to be canceled. The amendments are primarily editorial in nature, and support can be found throughout the specification and in the claims as originally filed, for example, page 6, lines 6-20 and original claim 1. Upon entry of the foregoing amendment, claims 1-5, 7-13 and 15-20 are pending in the application, with claim 1 being the independent claim. These changes are believed to introduce no new matter, and their entry is respectfully requested.

Based on the above amendment and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding rejections and that they be withdrawn.

I. Continued Examination Under 37 C.F.R. § 1.114

The Examiner acknowledged Applicants' request for continued examination and withdrew the finality of the previous Office Action. The Examiner also indicated that Applicants' submission filed on April 21, 2005 was entered. (*See* Office Action, page 2.)

II. Rejections under 35 U.S.C. § 102

The Examiner rejected claims 1-3, 6 and 15-20 under 35 U.S.C. § 102(b) as allegedly being anticipated by Jixian *et al.*, *Bull. Acad. Mil. Med. Sci.* 21:244-246 (1997)

(hereinafter "Jixian"). (See Office Action, page 3.) Applicants respectfully traverse this rejection.

The present invention is directed to method for obtaining human erythropoietin *comprising* culturing mammalian cells which express recombinant human erythropoietin in culture medium *consisting of* DMEM (Dulbecco's modified Eagle's medium), F12 medium, insulin and one or more additives selected from the group consisting of NaHCO₃, sugars, ethanolamine, pyruvate, amino acids and mixtures thereof.

The use of the transitional phrase "comprising" means that the claim is open, and encompasses elements not explicitly included in the claim, *e.g.*, additional steps, if it is a method claim. See *Genentech, Inc. v. Chiron Corp.*, 112 F.3d 495, 501 (Fed. Cir. 1997); *Georgia-Pacific Corp. v. United States Gypsum Co.*, 195 F.3d 1322, 1327-28 (Fed. Cir. 1999). Although the term "comprising" opens a method claim to the inclusion of additional steps, it does not affect the scope of the structure recited within the steps. See *Moleculon Research Corp. v. CBS, Inc.*, 793 F.2d 1261, 1271 (Fed. Cir. 1986), *rev'd on other grounds*, 872 F.2d 407 (Fed. Cir. 1989); *Phillips Petroleum Co. v. Huntsman Polymers Corp.*, 157 F.3d 866 (Fed. Cir. 1998).

The use of the phrase "consisting of" means the claim is closed, and "excludes any element, step or ingredient not specified in the claim." *Georgia-Pacific*, 195 F.3d at 1327-28. If the invention is claimed as "'consisting' of elements X and Y, it will not literally read on or cover a device with elements X, Y, and Z." 3 Chisum on Patents § 8.06[1][b][ii], 188-189 (March 2002). Therefore, it is clear that the presently claimed method can include additional steps in view of the use of the term "comprising," but that

the culture medium recited within the step only includes the recited elements, and nothing more, in view of the use of the phrase "consisting of."

Anticipation is established only if all the elements of an invention as stated in a claim are identically set forth or inherent in a single prior art reference. *See Transclean Corp. v. Bridgewood Services, Inc.*, 290 F.3d 1364 (Fed. Cir. 2002). Jixian discloses the production of recombinant human erythropoietin using CHO cells in a serum-free medium containing insulin (SFM-p). *See Abstract*. However, Jixian further discloses that SFM-p comprises DMEM:F12 (1:1) medium and various additives including Se, lipid, vitamins, peptone, transferrin and cytokines. *See Abstract*. In particular, Jixian teaches that SFM-p contains, in addition to basal medium DMEM:F12, additive A (casein hydrolysate and yeast extract), additive B (Se, ethanolamine and fatty acids) and additive C (insulin, transferrin and growth factors). *See Jixian translation, pages 4-5*.

Applicants acknowledge that Jixian discloses the use of some of the same culture medium components as those presently claimed. However, in contrast to the disclosure of Jixian, the *claimed* culture medium does *not* include, for example, transferrin, yeast extract, fatty acids or casein hydrolysate as additives. Since the elements of the claimed culture medium are closed by virtue of the phrase "consisting of," *i.e.*, only the recited elements may be in the culture medium and no more, and since Jixian discloses additional elements not recited in the claimed culture medium, the reference therefore fails to anticipate the claimed invention.

Moreover, the fact that the claimed invention does not employ any of these substances represents important advantages. The use of fewer additives makes the method more economical and easier to perform. In addition, the absence of these

additives allows for an easier purification procedure and analysis of the obtained product, since any of the aforementioned substances can leave contaminants with the erythropoietin, which would require much more sophisticated purification systems to remove. The corresponding loss of efficiency of the process would likely result in the recovery of much less mass of erythropoietin.

In reply to Applicants' arguments that Jixian fails to teach the claimed invention, the Examiner notes that

the features upon which applicant relies (i.e., absence of transferrin, yeast extract or casein hydrolysate as additives) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not to be read into the claims.

(Office Action, pages 5-6.)

Applicants note that by virtue of the "consisting of" language employed in claim 1, the features upon which Applicants rely, *e.g.* the absence of transferrin, yeast extract or casein hydrolysate as additives, *are* in fact recited in the rejected claims. Since the use of the consisting of claim language in the step excludes the addition of any unrecited elements within the medium, the absence of these additional elements is a *de facto* limitation of the claim.

In view of the above, it is clear that Jixian does not anticipate the claimed subject matter. Therefore, Applicants respectfully request that the rejection under 35 U.S.C. § 102(b) be withdrawn.

III. Rejections under 35 U.S.C. § 103

A. Claims 4, 5 and 13

The Examiner rejected claims 4, 5 and 13 under 35 U.S.C. § 103(a) as allegedly being obvious over Jixian in view of Koch *et al.*, EP Application No. 0 513 738 A2 (hereinafter "Koch"). (See Office Action, page 6.) Applicants respectfully traverse this rejection.

In order to establish a *prima facie* case of obviousness, there must be some suggestion or motivation, either in the cited references or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or combine reference teachings to obtain Applicants' invention. See *In re Rouffet*, 149 F.3d 1350, 1357 (Fed. Cir. 1998). There must also be a reasonable expectation of success. See *In re Vaeck*, 947 F.2d 488, 493 (Fed. Cir. 1991). Further, all of the claim limitations must be taught or suggested by the prior art references. See *In re Royka*, 490 F.2d 981 (CCPA 1974). The suggestion to make the claimed combination, as well as the reasonable expectation of success, must be found in the prior art references, and not in Applicants' disclosure. See *In re Vaeck*, 947 F.2d at 491.

Applicants assert that there is neither a suggestion nor motivation in Jixian or Koch to combine the teachings to obtain Applicants' invention. Moreover, even assuming, *arguendo*, that such a suggestion or motivation to combine the references is present, there would be no expectation of success in generating the claimed invention, and all of the claim limitations are not taught or suggested by the references.

As demonstrated above by Applicants, Jixian fails to disclose the claimed method. Koch clearly fails to remedy the deficiencies of Jixian.

Koch discloses the production of erythropoietin in a serum-free culture medium containing insulin by cultivating genetically engineered CHO cells. In addition, Koch discloses that, besides insulin, there are other substances that can affect the growth of mammalian cells, such as transferrin. *See* Koch translation at page 2, paragraphs 1 and 2. In order to avoid the use of animal proteins which can be contaminated with pathogenic viruses, Koch employs a water soluble iron compound, such as iron citrate, iron sulfate, iron chloride or potassium hexacyanoferrate, instead of transferrin in the culture medium. Therefore, a critical aspect of the Koch disclosure, aside from the addition of recombinant insulin from prokaryotes, is the addition of a water-soluble iron compound as a transferrin substitute. *See* Koch translation at page 2 and claim 1.

In contrast to the Koch disclosure, the present invention does not claim, among other things, a water-soluble iron compound as a substitute for transferrin in the culture medium (or indeed transferrin itself). Nevertheless, it is the Examiner's position that the presently claimed invention does not exclude water-soluble iron compounds:

in response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., water soluble iron compound to substitute for transferrin) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not to be read into the claims.

(Office Action, page 9.)

Applicants note that by virtue of the "consisting of" language employed in claim 1, the "features" upon which Applicants rely, *e.g.* the absence of a water-soluble compound to substitute for transferrin, *are* in fact recited in the rejected claims. Since

the use of "consisting of" excludes the addition of any unrecited elements, the absence of this additional element is an implicit limitation of the claim.

Clearly, the claimed invention is not taught or suggested by the prior art references. In fact, not only do Jixian and Koch fail to disclose the limitations of the claimed invention, but they in fact teach a person of ordinary skill in the art that there is not a reasonable expectation of success in producing recombinant EPO without transferrin or a substitute of transferrin as an extra source of iron in the cell culture medium.

Obviousness cannot be established by modifying the teachings of the prior art to produce the claimed invention unless there is some teaching, suggestion or motivation to do so found either in the reference itself or in the knowledge generally available to one of ordinary skill in the art. *See In re Fine*, 5 USPQ2d 1596 (Fed. Cir. 1988). Based on the disclosures of Jixian and Koch, there is no teaching, suggestion or motivation to use the claimed culture medium. In addition, the mere fact that the Jixian or Koch references could conceivably be modified to make the claimed invention does not render the resultant modification obvious unless the prior art also suggests the desirability of that specific modification. *See In re Mills*, 16 USPQ2d 1430 (Fed. Cir. 1990). The prior art references clearly fail to do so. Accordingly, it is respectfully requested that the rejection of claims 4, 5 and 13 under 35 U.S.C. § 103(a) be withdrawn.

B. Claims 7-10

The Examiner further rejected claims 7-10 under 35 U.S.C. § 103(a) as allegedly being obvious over Jixian in view of Yanagi *et al.*, *DNA* 8:419-427 (1989) (hereinafter

"Yanagi") and Chiba *et al.*, U.S. Patent No. 3,865,801 (hereinafter "Chiba"). (*See* Office Action, page 10.) Applicants respectfully traverse this rejection.

The Examiner must demonstrate, *inter alia*, that all the claim limitations are taught or suggested by the prior art references in order to establish a *prima facie* case of obviousness. Applicants reassert that neither Yanagi nor Chiba remedy the deficiencies of Jixian, in that they, alone or in combination, fail to teach the claimed method.

Nevertheless, it is the Examiner's position that "applicant's argumetns [sic] are found NOT persuasive because as stated above Jixian clearly teaches [the claimed invention]." (Office Action, page 12.) As demonstrated above, this argument is incorrect as Jixian does not teach the claimed invention. Therefore, Applicants submit that the Examiner has failed to establish a *prima facie* case of obviousness with respect to claims 7-10 and respectfully request that this rejection be withdrawn.

C. Claims 7, 11 and 12

In addition, the Examiner rejected claims 7, 11 and 12 under 35 U.S.C. § 103(a) as allegedly being obvious over Jixian, Yanagi and Chiba and further in view of van Reis, U.S. Patent No. 5,490,937 (hereinafter "van Reis"). (*See* Office Action, page 13.) Applicants traverse this rejection as well.

As discussed above, the cited art references must teach or suggest all of the claim limitations in order to establish a *prima facie* case of obviousness. Van Reis is directed to processes for separating compounds of interest from a mixture which comprises subjecting the mixture to tangential flow filtration where the filtration membrane has a specific pore size. As such, it is clear that van Reis fails to remedy the deficiencies of

Jixian, in that it does not, alone or in combination with Yanagi or Chiba, teach the claimed method. Accordingly, Applicants submit that the Examiner has failed to establish a *prima facie* case of obviousness of claims 7, 11 and 12 and respectfully request that this rejection be withdrawn.

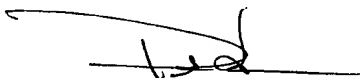
Conclusion

All of the stated grounds of rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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